WHAT IS CLAIMED IS:

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1. A method for inducing differentiation of an embryonic stem cell into an ectodermal cell, which comprises culturing the embryonic stem cell under non-aggregation conditions.

2 The method according to claim 1, wherein the ectodermal cell is a cell capable of differentiating into a nervous system cell or an epidermal system cell.

3. A method for inducing differentiation of an embryonic stem cell into an ectoderm-derived cell, which comprises culturing the embryonic stem cell under non-aggregation conditions.

4. The method according to claim 3, wherein the ectoderm-derived cell is a nervous system cell or an epidermal system cell.

5. The method according to claim 4, wherein the epidermal system cell is an epidermal cell.

6. The method according to claim 4, wherein the nervous system cell is a cell selected from the group consisting of the following (a), (b), (c) and (d):

(a) a neural stem cell;
(b) a nerve cell;
(c) a cell of neural tube; and
(d) a cell of neural crest.

7. The method according to claim 6, wherein the neural stem cell is a neural stem cell expressing nestin.

8. The method according to claim 6, wherein the nerve cell is a nerve cell selected from the group consisting of the following (a), (b), (c) and (d):

(a) a dopaminergic neuron;
(b) an acetylcholinergic neuron;
(c) a γ-aminobutyratergic neuron; and
(d) a serotonergic neuron.

9. The method according to claim 8, wherein the acetylcholinergic neuron is a motor nerve cell expressing islet 1.

10. The method according to claim 6, wherein the cell of neural tube is a cell selected from the group consisting of the following (a), (b), (c) and (d):

(a) a cell of neural tube before determination of dorso-ventral axis, which is capable of differentiating into a cell positioned at the ventral side by reacting with sonic hedgehog as a ventral factor of neural tube and of differentiating into a cell positioned at the dorsal side by reacting with bone morphogenetic protein 4 as a dorsal factor of neural tube;

(b) a cell of the neural tube ventral side, expressing HNF-3β (hepatocyte nuclear factor-3β) positioned on the basal plate of the most ventral side of neural tube;

(c) a cell of the neural tube ventral side, expressing a marker Nkx2.2 existing secondary to the HNF-3β (hepatocyte nuclear factor-3β) from the ventral side of neural tube; and

(d) a cell of the neural tube dorsal side, expressing Pax-7.

11. The method according to claim 6, wherein the cell of neural crest is a cell expressing AP-2 (activator protein 2).

12. The method according to any one of claims 1 to 11, wherein said culturing is carried out in the presence of bone morphogenetic protein 4.

13. The method according to any one of claims 1 to 12, wherein said culturing is carried out in the presence of sonic hedgehog.

14. The method according to any one of claims 1 to 13, wherein the non-aggregation conditions are conditions not mediating an embryoid body.

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15. The method according to any one of claims 1 to 14, which further comprises culturing under serum-free culture conditions.

16. The method according to any one of claims 1 to 15, wherein said culturing is carried out in the presence of a stroma cell-derived factor.

17. The method according to any one of claims 1 to 16, wherein said culturing is carried out in the presence of a stroma cell.

18. The method according to claim 17, wherein the stroma cell is a stroma cell whose proliferation potency is deleted by a physicochemical treatment.

19. The method according to claim 18, wherein the physicochemical treatment is selected from the group consisting of the following (a), (b) and (c):

(a) a treatment with an antitumor agent;

(b) a treatment by an radiation irradiation; and

(c) a treatment for tissue fixation used in pathologic diagnosis.

20. The method according to claim 19, wherein the antitumor agent is selected from the group consisting of mitomycin C, 5-fluorouracil, adriamycin and methotrexate.

21. The method according to claim 19, wherein the treatment for tissue fixation used in pathologic diagnosis is selected from the group consisting of a microwave fixation, a rapid freeze-substitution fixation, a glutaraldehyde fixation, a p-formaldehyde fixation, a formalin fixation, an acetone fixation, a Van fixation, a periodic acid fixation, a methanol fixation and an osmic acid fixation.

22. The method according to any one of claims 16 to 21, wherein the stroma cell is recognized by a monoclonal antibody produced by a hybridoma FERM BP-7573.

23. The method according to any one of claims 16 to 22, wherein the stroma cell is selected from the group

consisting of the following (a), (b), (c), (d), (e), (f) and (g):

(a) a fetal primary culture fibroblast;

(b) an SIHM mouse-derived STO cell;

(c) a mouse fetus-derived NIH/3T3 cell;

(d) an M-CSF deficient mouse calvaria-derived OP9 cell;

(e) a mouse calvaria-derived MC3T3-G2/PA6 cell;

(f) an embryonic stem cell-derived stroma cell; and

(g) a bone marrow mesenchymal stem cell-derived stroma cell.

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24. The method according to any one of claims 1 to 23, wherein the embryonic stem cell is selected from the group consisting of the following (a), (b) and (c):

(a) an embryonic stem cell established by culturing an early embryo before implantation;

(b) an embryonic stem cell established by culturing an early embryo produced by nuclear transplantation of the nucleus of a somatic cell; and

(c) an embryonic stem cell in which a gene on the chromosome of the embryonic stem cell of (a) or (b) is modified using a gene engineering technique.

25. The method according to any one of claims 1 to 24, wherein said culturing is carried out in the absence of retinoic acid.

26. The method according to any one of claims 1 to 25, wherein the embryonic stem cell is differentiated into an ectodermal cell or an ectoderm-derived cell at an efficiency of 5% or more.

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27. The method according to any one of claims 1 to 26, which does not substantially accompany differentiation induction of a mesodermal system cell.

28. A medium for inducing differentiation of an embryonic stem cell into an ectodermal cell or an ectoderm-derived cell, which is used in the method according to any one of claims 1 to 27.

29. A stroma cell-derived factor which induces differentiation of an embryonic stem cell into an ectodermal cell or an ectoderm-derived cell.

30. The factor according to claim 29, which is capable of adsorbing a mucopolysaccharide.

31. The factor according to claim 30, wherein the mucopolysaccharide is heparin.

32. An agent for inducing differentiation of an ectodermal cell into an epidermal system cell, which comprises, as an active ingredient, bone morphogenetic protein 4.

33. An agent for inducing differentiation of an embryonic stem cell into an ectodermal cell or an ectoderm-derived cell, which comprises, as an active ingredient, a stroma cell which has activity of inducing differentiation of an embryonic stem cell into an ectodermal cell or an ectoderm-derived cell, or a factor derived from the cell.

34. The agent according to claim 33, wherein the stroma cell is the stroma cell described in any one of claims 18 to 23.

35. The agent according to claim 34, wherein the stroma cell-derived factor is capable of adsorbing a mucopolysaccharide.

36. The agent according to claim 35, wherein the mucopolysaccharide is heparin.

37. A medium which comprises a culture supernatant obtained by culturing a stroma cell which has activity of inducing differentiation of an embryonic stem cell into an ectodermal cell or an ectoderm-derived cell in a medium comprising a mucopolysaccharide.

38. The medium which comprises a culture supernatant according to claim 37, wherein the stroma cell is the stroma cell described in any one of claims 18 to 23.

39. The medium which comprises a culture supernatant according to claim 37 or 38, wherein the mucopolysaccharide is heparin.

40. An agent for inducing differentiation of an ectodermal cell or an ectoderm-derived cell, which comprises, as an active ingredient, the culture supernatant described in any one of claims 37 to 39.

41. A method for obtaining an antibody which specifically recognizes a stroma cell which has activity of inducing differentiation of an embryonic stem cell into an ectodermal cell or an ectoderm-derived cell, which comprises using a stroma cell as an antigen.

42. The method according to claim 41, wherein the stroma cell is a stroma cell described in any one of claims 18 to 23.

43. An antibody which specifically recognizes a stroma cell which has activity of inducing differentiation of an embryonic stem cell into an ectodermal cell or an ectoderm-derived cell, which is obtained by the method according to claim 41 or 42.

44. A monoclonal antibody produced by a hybridoma FERM BP-7573.

45. A method for obtaining an antigen recognized by the antibody according to claim 43 or 44, which comprises using the antibody.

46. An antigen recognized by the antibody according to claim 43 or 44, which is obtained by the method according to claim 45.

47. A medium for culturing a cell, which comprises the antigen according to claim 46.

48. A method for obtaining a stroma cell-derived factor which has activity of inducing differentiation of an embryonic stem cell into an ectoderm-derived cell, which comprises using, as an index, the activity of inducing

differentiation of an embryonic stem cell into an ectodermal cell or an ectoderm-derived cell.

49. The method according to claim 48, which further comprises:

absorbing a mucopolysaccharide to a stroma cell-derived factor; and

recovering the stroma cell-derived factor from the factor absorbed on the mucopolysaccharide.

50. The method according to claim 48 or 49, wherein the stroma cell is a stroma cell described in any one of claims 18 to 23.

51. The method according to claim 49, wherein the mucopolysaccharide is heparin.

52. An ectodermal cell or an ectoderm-derived cell, which is induced by using the method according to any one of claims 1 to 27.

53. A method for increasing purity of a cell which is differentiation-induced from an embryonic stem cell, which comprises culturing the ectodermal cell or ectoderm-derived cell according to claim 52 in a medium comprising an antitumor agent.

54. The method according to claim 53, wherein the antitumor agent is selected from the group consisting of mitomycin C, 5-fluorouracil, adriamycin, methotrexate and ara-C.

55. A cell which is obtained by using the method according to claim 53 or 54.

56. A method for evaluating a substance relating to the regulation in a differentiation step from an embryonic stem cell into an ectodermal cell or an ectoderm-derived cell, which comprises:

carrying out the method according to any one of claims 1 to 27 in the presence of a substance to be tested and the method in the absence of the substance to be tested; and

comparing the differentiation step from an embryonic stem cell into an ectodermal cell or an ectoderm-derived cell in the presence of the substance to be tested with that in the absence of the substance to be tested.

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57. A method for screening a substance relating to the regulation in a differentiation step from an embryonic stem cell into an ectodermal cell or an ectoderm-derived cell, which comprises:

carrying out the method according to any one of claims 1 to 27 in the presence of a substance to be tested and the method in the absence of the substance to be tested; and

comparing the differentiation step from an embryonic stem cell into an ectodermal cell or an ectoderm-derived cell in the presence of a substance to be tested with that in the absence of the substance to be tested.

58. A method for evaluating a substance relating to the regulation of the function of an ectodermal cell or an ectoderm-derived cell, which comprises:

culturing the cell according to claim 52 in the presence of a substance to be tested and the cell in the absence of the substance to be tested; and

comparing the function of an ectodermal cell or an ectoderm-derived cell in the presence of the substance to be tested with that in the absence of the substance to be tested.

59. A method for screening a substance relating to the regulation of the function of an ectodermal cell or an ectoderm-derived cell, which comprises:

culturing the cell according to claim 52 in the presence of a substance to be tested and that in the absence of the substance to be tested; and

comparing the function of the ectodermal cell or the ectoderm-derived cell in the presence of the substance

to be tested with that in the absence of the substance to be tested.

60. A medicament comprising a stroma cell having activity of inducing differentiation of an embryonic stem cell into an ectodermal cell or an ectoderm-derived cell, or a factor derived from the cell.

61. The medicament according to claim 60, wherein the stroma cell is a stroma cell described in any one of claims 18 to 23.

62. The medicament according to claim 60, wherein the factor is capable of adsorbing a mucopolysaccharide.

63. The medicament according to claim 62, wherein the mucopolysaccharide is heparin.

64. A medicament comprising the antibody according to claim 43 or 44.

65. A medicament comprising the antigen according to claim 46.

66. A medicament comprising the cell according to claim 52 or 55.

67. The medicament according to any one of claims 60 to 66, which is a medicament for diagnosing, preventing and/or treating diseases caused by the ectoderm-derived cell.

68. The medicament according to claim 67, wherein the diseases caused by the disorder of an ectoderm-derived cell are diseases caused by the disorder of a nervous system cell or an epidermal system cell.

69. The medicament according to claim 68,

wherein the diseases caused by the disorder of a nervous system cell are Alzheimer disease, Huntington chorea, Parkinson disease, ischemic cerebral disease, epilepsy, brain injury, vertebral injury, motor neuron disease, neurodegeneration disease, pigmentary retinal dystrophy, cochlear hearing loss, multiple sclerosis,

amyotrophic lateral sclerosis or diseases due to a neurotoxin damage; and

the diseases caused by the disorder of an epidermal system cell are burn, wound, healing of wound, compression gangrene or psoriasis.

70. A method for immunologically detecting the antigen according to claim 46, which comprises using the antibody according to claim 43 or 44.

71. A tissue immunostaining method of the antigen according to claim 46, which comprises using the antibody according to claim 43 or 44.